



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
[www.uspto.gov](http://www.uspto.gov)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/817,913	08/06/2001	Zuomei Li	106101.145	8110
32254	7590	07/18/2007		
KEOWN & ZUCCHERO, LLP			EXAMINER	
500 WEST CUMMINGS PARK			VAKILI, ZOHREH	
SUITE 1200				
WOBURN, MA 01801			ART UNIT	PAPER NUMBER
			1614	
			MAIL DATE	DELIVERY MODE
			07/18/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/817,913	LI ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Zohreh Vakili	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 03 July 2006.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 45-48,50,51,53 and 54 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 45-48,50,51,53 and 54 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date: _____   | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION****Claims 45-48, 50-51, and 53-54 are presented for examination.**

A request for continued examination under 37 C.F.R. 1.114, including the fee set forth in 37 C.F.R. 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. 1.114, and the fee set forth in 37 C.F.R. 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 C.F.R. 1.114. Applicant's submission filed May 16, 2007 has been received and entered into the present application. Claims 45-48, 50-51, and 53-54 are pending and are herein examined on the merits.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 45-48 are rejected under 35 U.S.C. 102(b) as anticipated by Jones et al. (Nature Genetics, 1998, of record).

Claim 45 is directed to a method of modulating cell proliferation in a cell comprising the step of contacting the cell with an agent that inhibits one or more histone deacetylase isoforms. Claims 46-48 limit claim 45 to proliferation that is neoplasia and recite specific histone deacetylase isoforms.

Jones et al. disclose contacting a cell with TSA, a small molecule inhibitor of histone deacetylase. Jones et al. do not explicitly state that proliferation of the cells is inhibited, but the method of Jones et al. comprises all of the steps of the claimed method and, absent evidence to the contrary, would be expected to inhibit proliferation, including neoplastic proliferation.

Thus, Jones et al. disclose all limitations of and anticipate claims 45-48.

Claims 45-48, 50-51, and 53-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Kwon et al. (Proc. Natl. Acad. Sci. USA 1998, vol. 95, pages 3356-3361).

Claim 45 is directed to methods of inhibiting cell differentiation or proliferation; including neoplastic cell proliferation in an animal, by administering an agent that inhibits one or more specific histone deacetylase isoforms. Claims 46-48 limit claim 45 to neoplastic cell proliferation and recite specific histone deacetylase isoforms. Claim 50 is directed to a method of inhibiting neoplastic cell proliferation by administering a histone deacetylase small molecule inhibitor, optionally to a human and optionally in combination with an antisense inhibitor.

Art Unit: 1614

Kwon et al. disclose a small molecule inhibitor which inhibits histone deacetylase-I, which has the effect of inducing the reversion of cells transformed with a known oncogene from the morphology of a transformed cell to that of a normal cell.

Thus, Kwon et al. disclose all limitations of and anticipate claims 45-48, 50-51, and 53-54.

Claims 45-48 are rejected under 35 U.S.C. 102(e) as being anticipated by MacLeod et al. (US 2003/0078216).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim 45 is directed to methods of inhibiting cell differentiation or proliferation, including neoplastic cell proliferation in an animal, by administering an agent that inhibits one or more specific histone deacetylase isoforms. Claims 46-48 limit claim 45 to neoplastic cell proliferation and recite specific histone deacetylase isoforms.

MacLeod et al. disclose a method of inhibiting cell proliferation by inhibiting histone deacetylase using antisense oligonucleotides. MacLeod et al. further disclose that the antisense oligonucleotides are targeted to the histone

Art Unit: 1614

deacetylase isoforms recited in claim 47 and that the method may be performed in humans.

Thus, MacLeod et al. disclose all limitations of and anticipate claims 45-48.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1614

Claims 45-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sambucetti et al. (Journal of Biological Chemistry 1999, vol. 274, pages 34940-34947), Taunton et al. (Science 1996, cited on IDS), Baracchini et al. (US 5,801,154) and Bennett et al. (US 5,998,148).

Claim 45 are directed to methods of inhibiting cell differentiation or proliferation by administering an agent that inhibits one or more specific histone deacetylase isoforms. Claims 46-48 limit claim 45 to neoplastic cell proliferation and recite specific histone deacetylase isoforms.

Sambucetti et al. teach that inhibition of histone deacetylase using the tetrapeptide inhibitor TPX inhibits tumor cell proliferation. Sambucetti et al. do not teach the use of antisense oligonucleotide inhibitors of histone deacetylase.

Taunton et al. teach the isolation and sequence of histone deacetylase-I.

Baracchini et al. teach that antisense oligonucleotides can be used for research purposes, and also teach that preferred antisense oligonucleotides are modified in their sugar, backbone linkage and nucleobase composition (col. 6).

Baracchini teaches that such modifications are desirable in antisense oligos because these modifications have desirable properties such as enhanced cellular uptake, enhanced affinity for nucleic acid targets and increased stability in the presence of nucleases. Baracchini et al provide specific embodiments of such modifications at columns 6-8 and in Example 1. Tables 1-4 show the successful design and use of modified oligonucleotides in cells in culture. Table 1 exemplifies the successful practice of general antisense design taught at columns 8- 10. Column 4 teaches various carriers for antisense delivery.

Art Unit: 1614

Baracchini et al. also teaches at column 8 that antisense oligonucleotides are preferably 8 to 30 nucleotides and that it is more preferable to make antisense oligonucleotides that are 12 to 25 nucleotides in length. Baracchini is considered to comprise a detailed blueprint for how to make and use inhibitory antisense oligos to target any known gene.

The teachings of Bennett et al. are considered to parallel those of Baracchini et al. Bennett et al. teaches general antisense targeting guidelines at columns 3-4. Bennett et al. also teaches targeting 5'-untranslated regions, start codons, coding regions, and 3'-untranslated regions of a desired target. Bennett teaches, in column 5, for example, that antisense compounds are commonly used as research reagents and diagnostics. Column 5 indicates that antisense oligonucleotides 8-30 nucleotides in length are particularly preferred. Columns 6-7 teach that preferred antisense oligonucleotides contain modified internucleoside linkages including phosphorothioate linkages, among others. Columns 7-8 teach that preferred antisense oligonucleotides comprise modified sugar moieties including 2'-O-methoxyethyl. Bennett et al. also teach one of ordinary skill to modify nucleobases in antisense oligonucleotides, including the teaching of 5-methylcytosine (col. 8-9), and also to use chimeric antisense oligonucleotides (col. 9-10). Bennett et al. teach that the above modifications are known in the art to provide beneficial attributes to antisense oligonucleotides such as increased hybridization and nuclease protection, for example. Columns 10-24 teach numerous carriers for antisense oligonucleotides. Table 1 teaches the successful targeting of those regions taught in columns 3-4 with chimeric

Art Unit: 1614

phosphorothioate oligonucleotides having 2'-MOE (a 2'-O-methoxyethyl modification). Thus, Bennett et al. is also considered to comprise a detailed blueprint for how to make and use inhibitory antisense oligos to target any known gene.

It would have been obvious to one of ordinary skill in the art to use the cDNA sequence taught by Taunton et al. to generate antisense sequences as taught by Baracchini and Bennett for inhibition of histone deacetylase-I expression for the purposes of treating neoplastic cells via inhibition of histone deacetylase-1 as taught by Sambucetti et al.

One would have been motivated to create such compounds because Sambucetti et al. teach that their inhibitor of histone deacetylase can be used to inhibit tumor cell proliferation. Furthermore, both Bennett and Baracchini et al. teach that antisense molecules can be easily made and used to inhibit any target so long as the sequence is known, and provide for their methods of use in humans. Therefore, one of ordinary skill in the art would have been motivated to use the sequence histone deacetylase of Taunton et al. to develop antisense inhibitors for the purpose of treating neoplastic cells, because Sambucetti et al. teach that inhibition of histone deacetylase-I can inhibit tumor cell proliferation.

Finally, one would have a reasonable expectation of success given that Baracchini et al. and Bennett et al. provide a detailed blueprint for making and using modified antisense compounds targeted to a target gene, the sequence of which is provided by Taunton, and the steps of which are routine to one of ordinary skill in the art.

Thus in the absence of evidence to the contrary, the invention of claims 45-48 would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made.

Applicant's remarks have been fully and carefully considered in their entirety, but fail to be persuasive.

### **Conclusion**

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zohreh Vakili whose telephone number is 571-272-3099. The examiner can normally be reached on 8:30-5:00 Mon.-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1614

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Zohreh Vakili

Patent Examiner  
1614

July 3, 2007

*Ardin H. Marschel 7/14/07*  
**ARDIN H. MARSCHEL**  
**SUPERVISORY PATENT EXAMINER**